TABLE I. Urinary Excretion of Ascorbic, Dehydroascorbic and Diketogulonic Acids by Rats before and after Severe Temperature Shock.

Fraction	No. of analyses: Control	No. of analyses: Temperature shocked	Avg 24 hr excretion, μg with S.D.: Control	Avg 24 hr excretion, μg with S.D.: Temperature shocked	"F"
AsA	99	87	441 ± 136	485 ± 178	3.7
DHA	99	87	2 ± 5	43 ± 39	112 *
DKA	99	87	0 ± 0	48 ± 41	79 *

* Probability of variance ratio, "F," less than .01.

The animals were then placed in their individual cages and the excretion of AsA, DHA and DKA was determined each 24-hour period for 7 to 10 days following the mock temperature shock by the method previously employed(4). When the control excretion for each animal had been established, the experimental period began. Each animal was anesthetized with nembutal, and immersed to the neck in a water-bath held at 60°C for 15 seconds; the animals were replaced in their cages and the daily excretion of AsA, DHA and DKA determined for 7 to 10 days following the temperature shock. There were no fatalities during this period.

Results. The results obtained are summarized in Table I. As with cold environment and X-ray irradiation, exposure to this degree of temperature shock caused a marked increase in urinary excretion of DHA and DKA, which is highly significant. There was a slight increase in AsA excretion, which did not attain the level of significance.

Discussion. It appears that this third type of stress, which differs from the 2 previously reported in physiologic mechanism, has the same effect of increasing excretion of oxidized ascorbic acid in the urine. The physiologic mechanism responsible for this remains unknown. Attempts to demonstrate the adrenal glands and the kidneys as the site of formation have been unsuccessful(5).

Summary. 1. Adult albino rats were subjected to temperature shock by immersion in water at 60°C for 15 seconds. 2. Urinary excretion of dehydroascorbic and diketogulonic acids increased greatly over control values established before temperature shock.

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Cortisone on Oxygen Consumption of Granulation Tissue from the Rabbit. (20551)

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It has been shown that cortisone and adrenocorticotrophin (ACTH) produce an inhibitory effect on growth of granulation tissue in rabbits(1) and around turpentine abscesses in rats(2); that ACTH causes a retardation of wound healing in humans as studied by serial biopsies(3). Histological studies of the latter reveal a lack of fibroblasts, capillaries and ground substance; a condition not unlike that found in scorbutic animals(3). This suggests an inhibition of anabolic processes which are of primary importance in tissue repair. The literature reveals no data exist relative to the action of cortisone, ACTH, or adrenocortical extract (ACE) on the metabolism of granulation tissue. This report in-

dicates studies directed toward this end.

Materials and methods. Fifteen young male white rabbits weighing between 2.5 and 3.5 kg were divided into 3 groups. They were kept under laboratory conditions (20-27°C) for at least one week prior to experimental use. They were fed Pioneer Rabbit Food and water *ad libitum*. In the first 2 groups (A and B) granulation tissue was produced by sterile removal of a 9 cm^2 flap of shaved dorsal skin to a depth of 0.035-0.050 inches by means of a Brown electric dermatone.* The absence of hair follicles was considered indicative of sufficient penetration into the dermis. After the operation the area was covered with sterile vaseline gauze and a plaster cast. Group C, uninjured untreated control animals were subjected to a sham operation which consisted of shaving, use of vaseline gauze and a plaster cast comparable in size and location to the other experimental groups. Groups A and C had no further treatment; Group B received 25 mg of a stabilized saline suspension of 11-dehydro-17-hydroxycorticosterone acetate (Cortone, Merck) per day starting 3 days prior to injury and ending the day before tissue respirometry. All experimental animals were sacrificed 6 days after, either the surgical or sham procedure, by the injection of 50 cc of air into the marginal ear vein. Uninjured untreated control animals (Group C) were operated on immediately following sacrifice in order to obtain "normal" dermis. The granulation tissue or dermis was carefully dissected from the hypodermis. Various areas of the tissue were sliced by means of a Warburg cutter, the slices varied in thickness from 0.4 to 0.9 mm with a mean of 0.65 mm. This procedure was carried out on a chilled glass stage (3-5°C). The oxygen consumption of pooled slices was determined by the Warburg technic; at least 6 manometers were run on a given sample. The manometers were oscillated through an amplitude of 4 cm at a rate of 110 cycles/minute. Each respiration flask contained 0.2 ml 10% oxygenated NaOH solution in the central well, 2.8 ml oxygenated Krebs-phosphate (pH 7.4) solution(4) plus 65-100 mg of tissue in the main chamber. The manometers were gassed with 100% O_2 for 10 minutes and equilibrated at 37.5° ± 0.01°C for 15 minutes. The elapsed time between sacrifice of the animal and equilibration of the manometers was *ca* one hour. Manometric readings were taken for 60 minutes at 15-minute intervals. Samples of pooled tissue from each of the 3 groups were taken for wet and dry (17-20 hours at 105-110°C) determinations. The mean percent value for water content of given tissue samples was used to standardize the oxygen consumption in terms of QO_2, *i.e.*, mm^3 O_2 consumed/hour/mg (dry) of tissue.

TABLE I. Summary of Data for Oxygen Consumption (QO_2) of Dermis, "Normal" and Cortisone-Treated Granulation Tissue.

Groups	Untreated injured (A)	Cortisone treated injured (B)	Untreated uninjured control (C)
No. of animals	6	5	4
No. of exp.	52	32	22
True mean	−1.34±.06	−.45±.03	−.27±.02
% diff. compared to control dermis (C)	+396%	+67%	
SD	.46	.19	.10
P-value	<.01	<.01	

True mean = arithmetic mean ± its stand. error; SD = stand. deviation of indicated mean; P-value = probability value. Statistical analysis based on Student's method, where t = difference between a given pair of means/estimated stand. error of this difference.

Results. The various data for the oxygen uptake of granulation tissue (Group A and B) and dermis (Group C) are summarized in Table I. The true mean QO_2 values for the 3 groups are: (A) —1.34 ± 0.06, (B) —0.45 ± 0.03, and (C) —0.27 ± 0.02. A comparison of the mean QO_2 values for Groups A and B with C (control) shows that "normal" granulation tissue (A) gives a 396% increase ($P < 0.01$) and cortisone-treated granulation tissue (B) a 67% increase ($P < 0.01$). Cortisone-treated granulation tissue (B) shows a 66% decrease ($P < 0.01$) when compared with non-treated granulation tissue.

Discussion. Dermal slices from normal

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rabbits give a QO_2 of *ca* 0.3 under the experimental conditions prevailing. This may be compared with the only other known value of 0.9 for "strips of skin" of very young rats(5). The difference between these two values may be due to a species variation; however, "strips of skin" included epidermis which was absent in our study. This may suggest that a considerable difference exists between the oxygen consumption of epithelial and connective tissues. As expected there is an increase (+396%) in the endogenous metabolism of granulation tissue (Group A) compared with dermis (Group C) from the corresponding area of rabbits. The metabolism and water content of young "normal" cells are consistently higher than of older cells(6). However, the histological organization of granulation tissue and of dermis is not exactly comparable. The chief difference is not only smaller numbers of actively proliferating cells and capillaries, but also the almost complete absence of polymorphonuclear leucocytes in the latter. Therefore, it is suggested that the increase in oxygen consumption may be due not only to the presence of larger numbers of younger cells, but to different cell types found in granulation tissue as compared with dermis. A comparison of the oxygen uptake of cortisone-treated (Group B) with non-cortisone treated granulation tissue (Group A) shows a significant decrease (66%). This suggests that cortisone exerts an inhibitory action on the oxygen consumption of granulation tissues. Since this tissue is composed of various cell types, it further suggests that cortisone may inhibit the growth (anabolic) processes in one or more of the component cells, *e.g.*, fibroblasts, clasmatocytes or endothelial cells. It has been shown that whole adrenocortical extract (ACE) and corticosterone, when incubated with liver and brain slices from normal rats, inhibit oxygen consumption(7). Thus it appears that the cortisone fraction of ACE is probably not specific in its metabolic depressant action. The mechanism of this inhibitory action has not yet been elucidated. Further experiments are underway in this laboratory.

Summary. The oxygen consumption (QO_2) of pooled dermal and granulation tissue slices from 2.5-3.5 kg male white rabbits were studied by the Warburg technic. The rabbits were divided into 3 groups: (A) Those subjected to dermal injury. (B) Those subjected to dermal injury, but in addition receiving pre- and post-operative cortisone treatment, *i.e.*, 25 mg/day. (C) Those animals subjected to a sham operation. 1. "Normal" uninjured dermal slices give a mean endogenous QO_2 value of 0.27 ± 0.02 (Group C, Table I). 2. Slices from untreated granulation tissues (Group A) show an increase of 396% over their control (Group C). 3. Slices from cortisone-treated granulation tissue (Group B) give only a 67% increase over the control (C), or a 66% decrease when compared with untreated granulation tissue(A). 4. The implications of these results are discussed.

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